

# Variations of Intrathoracic Amount of Blood as a Reason of ECG Voltage Changes

Marina Saltykova, Ph.D., Andre Capderou, M.D., Ph.D.,\* Oleg Atkov, M.D., Victor Gusakov, M.S.,† Gennagiy Konovalov, M.S.,† Leonid Voronin, M.D.,† Rustem Kaspranskiy, M.D.,† Valeriy Morgun, M.D.,† Olivier Bailliart, M.D., Ph.D.,‡ Milan Cermack, M.D.,\*\* and Pierre Vaïda, M.D.‡‡

From the Cardiology Research Complex, Moscow, Russia; \*UPRES EA2397, CCML, University Paris XI, France; †Gagarin Cosmonauts Training Center, Russia; ‡EFR Lariboisière Hospital, Paris, France; \*\*University, Zurich, Switzerland; ‡‡Physiology, Aerospace Medicine, University Bordeaux 2, France

**Background:** It is known that electroconduction of intrathoracic organs and tissues significantly influences the ECG voltage. It changes during therapy or exercise test due to redistribution and/or volume variations of blood and body fluids and their electroconductivity variations. This fact must be taken into consideration during interpretation of corresponding ECG. But there are no quantitative estimations of this influence on human ECG. The goals of this study were to estimate the influence of variations of thoracic electroconduction, and heart volume on QRS voltage in humans, due to gravity change.

**Methods:** ECGs of 26 healthy volunteers were analyzed in upright and supine position. Experimental conditions—acute change of gravity—are created in a special aircraft flying on Kepler's parabola trajectory. Each parabola includes phases of normo-, hypergravity (blood shifts in caudal direction), and microgravity (blood redistributes in cranial direction). Amplitude of QRS in Frank leads in all phases has been analyzed. 2-D echo studies for six subjects were used for estimation of heart volume change.

**Results:** In an upright position during hypergravity the amplitude of R wave in Z increases in 95% of cases (mean 0.19 mV). During microgravity amplitude of R wave in Z decreases in 95% (mean 0.24 mV). In supine position changes of QRS voltage are not significantly.

**Conclusion:** Blood redistribution during gravity change leads to changes of QRS voltage, which is more expressed and steady on R in Z lead: an average near 0.2 mV. It is due to the balance between two factors: (a) changes of degree of short circuiting by variations in the amount of blood in thorax (b) changes of distance between heart and electrodes as a result of change in the position, form, and volume of the heart.

**A.N.E. 2003;8(4):321–332**

human ECG; QRS voltage; blood redistribution; gravity changes

ECG is a traditional method for observation of electrical heart activity. It is easy to use, but there are still some problems with the physiological interpretation of changes of ECG parameters. Several factors, which do not depend on the electric activity of the heart, exert a significant influence on the ECG voltage. The most important factor is the electroconduction of intrathoracic organs and tissues.<sup>1–14</sup> This fact is not always taken into consideration during ECG analyses and interpretation, especially in

monitoring ECG during therapy or exercise test. On the one hand, it takes place in most cases and, on the other, small and steady ECG voltage variations (0.1–0.2 mV) are taken into consideration in this monitoring.<sup>15</sup> But many researchers<sup>2–8</sup> have shown the importance of thorax electroconduction using analytical models and in experiments on animal opened chest. But there are large problems in the estimation of the influence of this factor on human ECG in clinical conditions; it is very difficult

---

*This study was a part of the project INTAS-ESA 99-01319 (Co-ordinator, Pierre Vaida).*

*Address for reprints: Marina Saltykova, Department of Advanced Diagnostical Methods, Cardiology Research Complex, 3-ya Cherepovskaya, 15A, Moscow 121552, Russia. Fax: 007 095 414 66 99; E-mail: MarinaMS2002@mail.ru*

to distinguish the influence of electroconduction from other factors. For human ECG there are single studies only: Rudy et al.<sup>11</sup> have shown the significant influence of lung electroconductivity on ECG voltage in clinical condition; Vitolo et al.<sup>12</sup> have shown that variation of electroconductivity can be a reason for the inverse relation between ECG voltage and cardiac volume during hemodialysis, contrary to traditional electrocardiography criteria that directly relate ECG voltage and cardiac volume. Lepeshkin<sup>1</sup> propounded a thesis about changing electroconduction (change of short circuit degree in myocardial wall) as a mechanism that connects change of QRS voltage and acute blood pressure change. It could be especially important in cases of ECG monitoring during antihypertensive therapy. Analogical mechanism can be used for an explanation of "unclear mechanism"<sup>16</sup> of QRS voltage change during the exercise test without left ventricular volume change<sup>15</sup> and without coronary artery disease<sup>17</sup> or during the experimental myocardial ischemia.<sup>18</sup>

For estimation of the electroconduction influence on voltage of human ECG an acute change of electroconduction is needed, so that other factors, which influence ECG voltage (ion concentration in myocardium or thickness of myocardial wall, for example), do not have enough time for significant change. Acute change of human thorax electroconduction can be evoked by changing the amount of blood or the amount of air in the thorax. In vivo acute air alternation takes place during the breathing test. But in this case alternation of the amount of blood also takes place. An increment of blood (high electroconduction substance) flow in right atria and ventricular and an increment of the amount of air (low electroconduction substance) in lung have an influence on thorax electroconduction in different directions,<sup>19</sup> and the balance of these factors is variable. Therefore, blood redistribution is more adequate for studying the influence of electroconduction of intrathoracic organs and tissues on ECG. In vivo it can be made by two ways: (1) rotation of the body in the head down direction, it leads to blood shift in the cranial direction, and (2) change of gravity, which leads to blood shifts in the caudal direction in hypergravity and in the cranial direction in microgravity. Acute changes of gravity are created in a special aircraft flying on Kepler's parabola trajectory. Each parabola includes phases of normo-, hypergravity (blood shifts in caudal direction), and microgravity (blood redistributes in cranial direc-

tion). The second way allows analysis of two opposite situations: decrement of thorax electroconduction in hypergravity and increment of thorax electroconduction in microgravity. Besides, in a rotation body in the head down direction, alteration of the heart position is bigger in comparison with the microgravity condition, because in this situation there is shift of heart in the cranial direction due to the force of gravity but in the microgravity force is weak. It is clear that all heart shifts are very small relative to heart size.

The goals of this study were: (1) to estimate, in humans, the influence on QRS voltage of variations of thoracic electroconduction and heart volume, due to gravity change; and (2) to find QRS parameters that mainly depend on each factor.

Only QRS parameters are discussed in this study, because ECG parameters of depolarization are steadier when they are compared to repolarization. The parameters of repolarization depend on duration of action potential and, hence, on the stretching of fibers, heart rate, and other factors. By contrast, the amplitude of action potential of normal ventricular cardiomyocyte is constant, because it does not depend on values of mild stretching, heart rate (if HR is less than 350 beats/min), and acetylcholine, and catecholamines influences.<sup>20-23</sup> Two to three seconds are needed for transition from normal gravity to mild hypergravity, or from mild hypergravity to microgravity. This period is too small for significant change of ion concentration. From these facts, QRS voltage variations in this study are evoked by variations of changing of electroconduction of intrathoracic organs and tissues and faint alteration of form, volume, position of heart and rib cage.

## MATERIAL AND METHODS

### Subjects

ECGs of 26 healthy volunteers (2 females and 24 males) aged between 22 and 52 years (mean  $\pm$  SD:  $39.0 \pm 9.25$ ) and free of any cardiac pathology, were analyzed in this study. All subjects underwent the special flight physical examination and gave written informed consent to participate in this study. Subjects did not take any medication before and during the flights. This study was approved from an ethical point of view by the Comité Consultatif pour la Protection des Personnes en Recherche Biomédicale (CCPPRB) Bordeaux A, the French Space Agency (Centre National d'Etudes

Spatiales, CNES), the European Space Agency (ESA) medical board, and Bio-Medical Ethical Committee of Gagarin Cosmonauts Training Center in Star City, Russia.

Voltage parameters of QRS: amplitude of waves Q, R, S in leads X, Y, Z have been analyzed in this study.

### Equipment and Protocol

Experimental conditions—acute change of gravity—are created in a special aircraft flying on Kepler's parabola trajectory.<sup>24–26</sup> The ascending phase of the parabola (20 seconds) is associated with mild hypergravity (1.7–1.8 G), resulting in blood shifts to the lower extremities and in the elongation of the heart into a stretched form. The next 20 seconds correspond to the upper part of the parabola. This is the microgravity (0 G) period, characterized by redistribution of blood to upper body parts (near 500 ml)<sup>25</sup> and faint alteration of rib cage.<sup>27</sup>

The ECG material consists of three parts that were registered when the subjects were in following positions:

- I – in upright position (44 cases);
- II – in upright position with the equipment for the creation of low body negative pressure (LBNP), which allows decrease of blood redistribution in microgravity, when blood shifts in the cranial direction (26 cases);
- III – in supine position (8 cases).

In order to keep a near standing position during microgravity, the subjects were attached to a saddle with a seat belt and had their feet secured in a foot strap.

The flights were organized by CNES, ESA, and NOVESPACE (trade society of CNES, France) at the Société Girondine d'Équipements, de Réparation, et de Maintenance Aéronautique (SOGERMA) center in Bordeaux, France and Gagarin Cosmonauts' Training Center in Star City, Russia, during 1997 to 2001.

ECGs of 23 volunteers had been registered in the flight of the CNES-AIRBUS A300 ZERO-G aircraft using a digital (500 Hz, 12 bits) recording with classical 10 electrodes—12-lead ECG plus four additional electrodes for orthogonal leads X, Y, Z (Cardionics, Bruxelles, Belgium). ECGs of three volunteers had been registered in flights of the aircraft IL-76 MDK with a digital (500 Hz, 12 bits) 12-lead

ECG cardioregistrator (Geolink, Moscow, Russia). In these cases seven electrodes were placed according to the definition of a Frank lead system and three electrodes were situated on the left and right hands and on the right foot. Frank formulas were used for computerized calculation of X, Y, Z leads.<sup>28</sup>

Gravity variations during a parabolic flight profile include five consecutive phases:

1. Normogravity (1 G): first steady state before beginning the parabola.
2. First period of mild hypergravity (1.7–1.8 G): pull-up during the ascending phase of the parabola, 20–25 seconds.
3. Microgravity (0 G): corresponding to the upper part of the parabola, 20–25 seconds.
4. Second period of mild hypergravity (1.7–1.8 G): pull-out during the descending phase of the parabola, 20–25 seconds.
5. Normogravity (1 G): second steady state just after the end of the parabolas.

In this study we analyzed and compared only flight phases 1, 2, and 3. ECG from each subject was recorded during several parabolas (from 2 to 20). For every parabola triplets of QRS complexes were made using all normal QRS of normogravity (phase 1), hypergravity (phase 2), microgravity (phase 3). Voltage parameters of QRS: amplitude of waves Q, R, S in leads X, Y, Z have been calculated for meaning QRS of normogravity, hypergravity, and microgravity by traditional the ECG manner as a value of maximal divergence from isoelectric baseline.

In addition, the amplitude of the waves of QRS for every heart beat and heart rate (RR duration) were also analyzed.

Experimental data were collected in nine flight campaigns and in two different aircrafts; eight flight campaigns (792 parabolas for 23 volunteers (from 2 to 20 parabolas for each volunteer in one flight)) in the A300 Zero-G and one flight campaign (16 parabolas for 3 volunteers (from 2 to 7 parabolas for each volunteer in one flight)) in the IL-76 MDK. There were slight differences in the body position and placement of the electrodes. In the first and second campaigns the saddle and the arm support design was used, which was different in other campaigns. From the fifth up to the eighth campaigns, echocardiography was used and electrode V4 was shifted to the left, to clear this space for the echo-detecting element. In the campaign number 9, flown in IL-76 MDK, electrodes were in Frank

position and the saddle was somewhat different from the previous campaigns. But this was not of specific interest in this study because we did not analyze the values of the amplitudes of QRS waves by themselves, but their relative changes (increment or decrement) during parabolic flights.

Eight subjects participated in several flights (2 subjects took part in 5 flights, 1 subject took part in 4 flights, 3 subjects took part in 3 flights, 2 subjects took part in 2 flights). Twenty-six cases (17 subjects: 3 subjects took part in 3 flights, 3 subjects took part in 2 flights, 11 in 1 flight) were studied with and without the special equipment for creating negative pressure (–50 mmHg) in lower body negative pressure (LBNP). This equipment allows decrease in blood redistribution in microgravity. The LBNP was carried out in a box with the subject in an upright position<sup>26</sup> and was applied only during microgravity.

Eight cases (6 subjects: 2 of 6 ones took part in 2 flights) were studied in both supine and upright positions.

For estimation of heart volume change data of 2-D echo studies were used. They were performed using a regular ASPEN, Acuson machine. End diastolic frames were selected and end diastolic volume of left ventricular were manually traced using the trackball by two independent observers.

### Statistical Analysis

The target of statistical analysis in this study was the revealing QRS changes typical for humans in different phases of parabolic flight. In this study we did not take into consideration repetition of subjects in different flights, because the condition for ECG recorded was not absolutely equivalent in different flights and the time between the flights was more than half a year.

For taking into consideration a large variety of QRS voltage changes during changes in the gravity condition and for choosing the most typical changes (changes took place in most subjects' ECG) we made a statistical analysis of QRS voltage changes in upright position in two stages:

Stage I—Revealing significant Q, R, S voltage changes due to gravity changes for each case separately. The case is a subject's ECG during several following parabolas (from 2 to 20)). It was necessary because, on the one hand, in normogravity QRS voltage is different in subjects as a consequence of anatomic and physiological differences,

and on the other, ECGs were recorded during different numbers of parabolas (from 2 to 20). In this stage pair comparison of amplitudes of Q, R, S in hypergravity and normogravity, and in microgravity and normogravity was done for a sequence of parabolas of each case. If the number of parabolas, in which ECG was recorded, was more than 5, the Wilcoxon paired test was used for the determination of the statistical significance of amplitude changes. In other cases (4 cases) the variation of Q, R, or S amplitude was recognized as significant if this variation took place in all the parabolas (i.e., in 3–5 parabolas). Result of stage I were a determination of the list of QRS parameters (for every case separately), which change significantly due to gravity change.

Stage II—Revealing Q, R, S voltage changes typical for human ECG in different phases of parabolic flight. Changes in Q, R, S amplitudes were named typically if they were similar for most subjects; that is, they were statistically significant in most cases. The binomial criterion was used to determine the statistical significance with the level of significance of  $P < 0.05$ . For QRS parameters that typically change due to gravity change, median, mean, standard deviation, and minimal and maximal value of their changes (increase or decrease) were calculated. Results of stage II were (1) a list of QRS parameters, which changes statistically in most subjects' ECG (by binomial criterion); and (2) calculation of statistical characteristics of these QRS parameters changes.

In this study we did not analyze the statistical significance of differences between statistical estimation of group mean values for every phase of parabolic flight because the variation of QRS parameters of one subject between the different phases is smaller than the variation of QRS parameters of all subjects in one phase. In other words: inter-group dispersion in one phase of parabolic flight is bigger than the variation between different phases for one subject.

For statistical estimation of changes of the left ventricular ending diastolic volume the Wilcoxon criterion was used. For comparison of changes of QRS parameters in parabolas with LBNP and without LBNP the following approach was used:

1. For every case statistical significance (by the Mann-Whitney *U*-test) of QRS parameter differences between parabolas with LBNP and without LBNP was determined separately.

2. The binomial criterion was used for checking of hypothesis: "these changes are typical, i.e., they take place in statistically most cases."

## RESULTS

In this article we present typical changes of QRS parameters in different phases of parabolic flight without individual peculiarities. As a result of the statistical analysis of QRS parameters (see above), the following regularities are revealed.

### Typical Changes of QRS Voltage in Upright Position

Changes of amplitude of R wave in Z and X leads are similar for most subjects, but other parameters of QRS have considerable variations for different subjects. Usually, the amplitude of R wave in Z is located between the 60 ms and 70 ms from the beginning of QRS (Fig. 1). Rz corresponds to the potential from the back-basal region of myocardium. Rx amplitude, which is located between the 35th ms and 50th ms from the beginning of QRS, corresponds to the excitation of apex.

Statistical characteristics of changes of R amplitudes in Z in hyper- and microgravity relative to normogravity are shown in Table 1. They were cal-

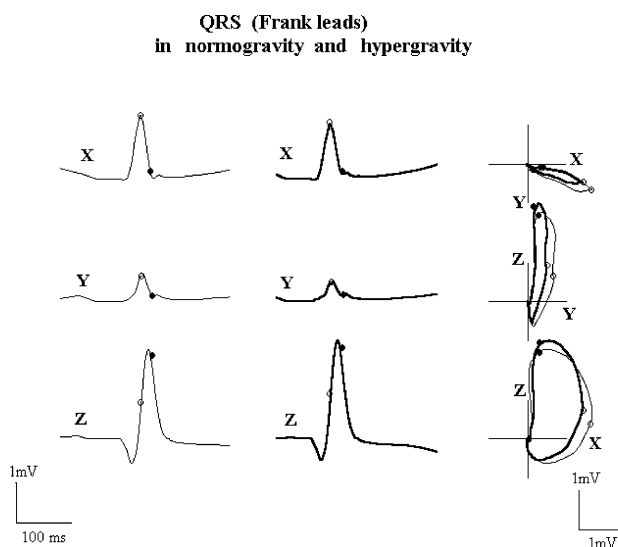
culated for increase (in hypergravity) and decrease (in microgravity). In the last column there are a number of cases in which change of R amplitude in hypergravity relative to normogravity was statistically significant. In every case statistically significance was calculated by Wilcoxon test or its analog (see Statistical Analysis).

(a) *Comparison of QRS voltage in mild hypergravity with normogravity.* During mild hypergravity the amplitude of R wave in Z increases in comparison with normogravity in 95% of the cases (42 of 44,  $P < 0.01$  (binomial criterion)). The mean increment is  $0.19 \pm 0.011$  mV. There were two exceptions: during one of four flights of one subject and during one of three flights of other subject, the changes of Rz wave amplitude in mild hypergravity did not differ significantly. A representative example of QRS changes in mild hypergravity in comparison with normogravity is shown in Figure 1. It is to be noted that amplitude change takes place from the first heart beats of hyper-gravity. Representative graphics of R-wave amplitude in Z beat-to-beat is shown in Figure 2. In lead X, the amplitude of the R wave in mild hypergravity, relative to normogravity, decreases significantly in 12 and increases in 4 of 44 cases. In lead Y, the amplitude of R wave in mild hypergravity, relative to normogravity, increases in 9 of 44 cases, and decreases in 5 cases.

(b) *Comparison of QRS voltage in microgravity with normogravity.* During microgravity in comparison with normogravity the amplitude of R wave in Z decreases in 95% of the cases (42 of 44,  $P < 0.0101$  (binomial criterion)). This means that in microgravity, the relative contribution of the potential from the back-basal region of myocardium decreases. Mean decrement is  $0.24 \pm 0.018$  mV. A representative example of QRS changes in microgravity relative to normogravity is shown on Figure 3. There were two exceptions: during one of five flights of one subject and during the flight of other subject, the changes of R wave amplitude in microgravity did not differ significantly.

It is necessary to note that amplitude change took place from the first heart beats of microgravity, but the heart rate change took place after about a 2-second delay. Representative graphics of R amplitude in Z and corresponding RR are shown in Figure 4.

Besides in 80% of the cases the amplitude of R in all leads in first heart beats was less than in the following beats.



**Figure 1.** Representative example of QRS waves in X, Y, Z leads and QRS loops in frontal, sagittal, and horizontal planes in upright body position. Thin lines in 1 G; bold lines in 2 G. White disks correspond to 45 ms from beginning of QRS; black disks correspond to 65 ms from beginning of QRS.

**Table 1.** Change of R Amplitude in Z during Hypergravity and Microgravity, Relative to Normogravity

	Median	M	SD	Min	Max	N	P
Hypergravity							
Increase							
mV	0.16	0.19	0.11	0	0.65	42	<0.01
%	12	16	11.9	0	56	(95%)	
Microgravity							
Decrease							
mV	-0.20	-0.24	0.20	0	-1.07	42	<0.01
%	-15	-18	11.9	0	-49	(95%)	

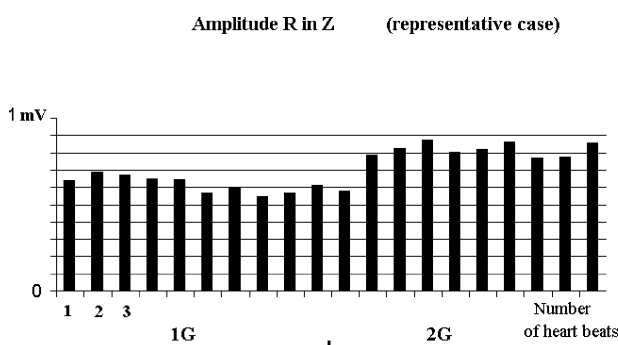
M: mean; SD: standard deviation; N: number of cases with statistically significant changes.

Statistical characteristics of change in R amplitudes in X in microgravity relative to it in normogravity are shown in Table 2.

In lead X, the amplitude of R wave in microgravity, relative to normogravity, increases significantly in 25 of 44 cases (57%), and decreases in 2 cases. In lead Y, the amplitude of R-wave in microgravity, relative to normogravity, decreases in 17 of 44 cases, and increases in 11 cases.

### Typical Changes of Left Ventricular Volume in Upright Position

Six subjects were studied in upright position by 2-D echo. The values of mean (M) and standard deviation (SD) of left ventricular volume for normogravity (1 G), mild hypergravity (2 G), and microgravity (0 G) are shown in Table 3. In different phases of parabolic flight left ventricular volume changes do not exceed 10–30%.

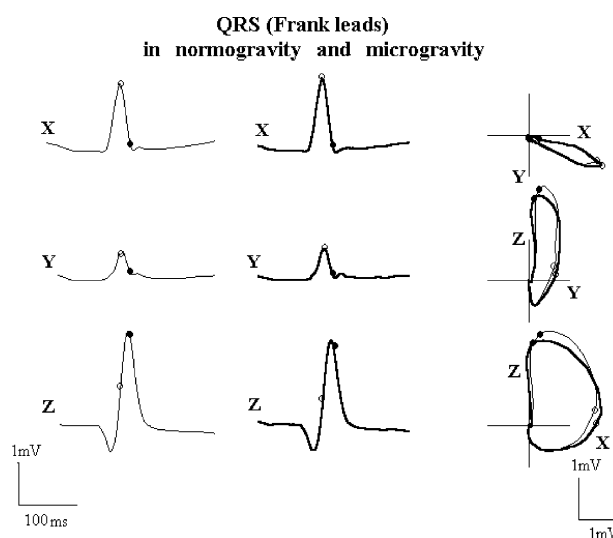


**Figure 2.** Representative graphics of changing of R wave (in mV) in Z beat-to-beat in hypergravity relative to normogravity. The X axis—number of heart beats; the Y axis—voltage of R wave.

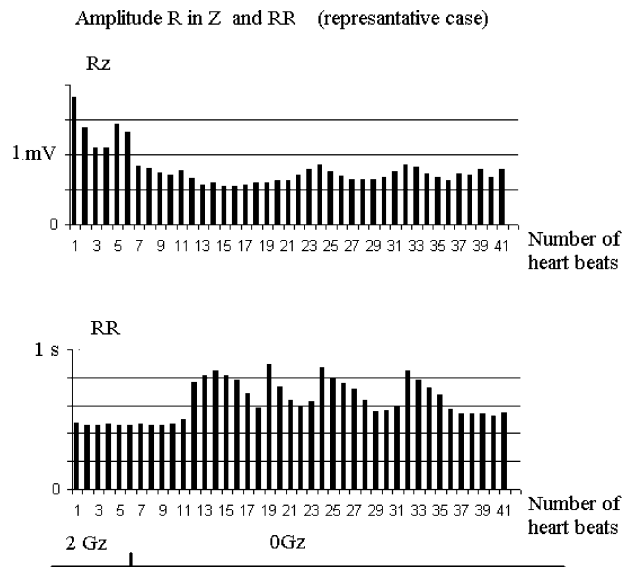
### Dependence of QRS Voltage Changes on Presence of LBNP in an Upright Position

Twenty-six cases were studied with and without LBNP. The statistical characteristics of change in R amplitudes in Z in microgravity with LBNP relative to normogravity and relative to microgravity without LBNP are shown in Table 4.

In 18 of 26 cases (69%), R amplitude in Z is smaller in microgravity with LBNP relative to normogravity. In 14 of 26 cases (54%), during the employment of LBNP, R amplitude in lead Z is significantly greater with LBNP than without it.



**Figure 3.** Representative example of QRS waves in X,Y,Z leads and QRS loops in frontal, sagittal, and horizontal planes in upright body position. Thin lines in 1 G; bold lines in 0 G. White disks correspond to 45 ms from beginning of QRS; black disks correspond to 65 ms from beginning of QRS.



**Figure 4.** Representative graphics of R amplitude in Z (in mV) and corresponding RR (in seconds) in microgravity and preceding period of hypergravity. The X axis—number of heart beats; the Y axis—voltage of R wave (for Rz) and value of RR interval (for RR).

In 12 of 26 cases (46%), during the employment of LBNP, R amplitude in lead X is smaller with than without LBNP. In 14 of 26 cases (54%) R amplitude in X is greater in microgravity without LBNP relative to normogravity, but in microgravity with LBNP this regularity was not observed. It means that the application of LBNP in microgravity leads to decreasing influence of gravity change on R voltage in Z and X. Without LBNP, the voltage variations are greater.

During the employment of LBNP, R amplitude in lead Y is smaller in 10 of 26 cases (38%) with than without LBNP, but larger in 2 of 26 cases (8%). In 11 of 26 cases (42%), R amplitude in Y is smaller in microgravity without LBNP relative to normogravity and larger in 7 of 26 cases (27%), during micrograv-

ity with LBNP, R amplitude in Y is smaller in 11 of 26 cases (42%) relative to normogravity and larger in 2 of 26 cases (8%).

It means that application of LBNP in microgravity does not definitely influence voltage in Y.

### Dependence of QRS Changes on Body Position (Upright-Supine)

Eight cases were studied in upright and supine positions. The statistical characteristics of changes of amplitude R in Z in hyper- and microgravity relative to normogravity are shown in Table 5. Changes of amplitude R in X and Y in hyper- and microgravity relative to normogravity are not significant analogically to R in Z.

The most typical changes of QRS in upright position are not expressed in the supine position.

## DISCUSSION

It is well known that acceleration induces voltage changes in QRS,<sup>29,30</sup> but adequate explanations of this fact are lacking. During acute variations of gravity only some factors change significantly; the other factors are relatively constant and their influence on QRS voltage variations cannot be taken into consideration. For example, blood resistance is almost constant. The main contribution to blood resistance is linked to the resistance of blood cell membranes.<sup>2,7,10</sup> Consequently it depends mainly on the number of blood cells in a given volume. Serum albumin level influences blood resistance as well.<sup>31</sup> Because there is not enough time for significant changes in these factors in our experiments, blood resistance could be considered to be constant.<sup>32</sup> Also, the amplitude of action potential of myocardial cells does not change during the parabolic flight, because in normal ventricular

**Table 2.** Change of R Amplitude in X During Microgravity, Relative to Normogravity

	Median	M	SD	Min	Max	N	P
Increase							
mV	0.2	0.23	0.17	0.01	0.6	25	NS
%	11	14	10.6	1.2	50	(57%)	
Decrease							
mV	-0.08	-0.12	0.12	-0.46	0.01	2	NS
%	-4.3	-5.3	4	-14	-0.4	(5%)	

M: mean; SD: standard deviation; N: number of cases with statistically significant changes.

**Table 3.** The Values (Mean and Standard Error) of End Diastolic Volume during different Phases of Parabola

Persons	Normogravity	Hypergravity	Microgravity
CM	111.8 ± 0.9	100.8 ± 1.7*	146.9 ± 5.03*
JLL	116.9 ± 1.7	94.5 ± 1.03*	129.6 ± 0.72*
JM	130.0 ± 2.36	114.6 ± 2.24*	154.7 ± 1.18*
LL	155.9 ± 1.22	139.1 ± 1.19*	182.8 ± 5.95*
SB	87.1 ± 0.76	74.1 ± 0.91*	93.3 ± 1.63*
PV	125.4 ± 3.75	92.3 ± 4.35*	132.7 ± 3.44

\*Difference from corresponding value in 1 G (see statistical section); P < 0.05.

it is not dependent on mild stretching, heart rate (less than 350 beats/min), and acetylcholine, and catecholamines influence.<sup>20–23</sup>

Apparently the following four factors have a major influence on QRS variations during gravity changes:

1. Electroconduction of tissues located between the heart and the electrodes;<sup>1,2,9,11,14,19,33</sup>
2. Electroconduction of myocardium. This depends on electroconduction of cardiac fibers, and on the amount of blood in myocardium and in the ventricles;<sup>1–8,10,13,14,34–36</sup>
3. Distances between the heart and electrodes as a consequence of the heart position, form, volume changes, and changes of chest form;<sup>1,2,9,12–14,33,34,37,38</sup>
4. Nonhomogeneity of the heart, which changes with variations of the heart volume (Brody effect).<sup>9,11–13,36</sup>

*First factor.* Resistance of blood is smaller than resistance of intrathoracic organs and tissues.<sup>1,2,9,11,14,36</sup> Therefore, during the parabolic flight, when blood shifts in the cranial direction (in microgravity), the resistance of intrathoracic organs and tissues decreases. As a result, the effect of short circuit in the thorax increases with consequent decrease in ECG voltage.<sup>1,33</sup> By analogy, shift of blood in the caudal direction (in mild hypergravity) results in increase in the resistance of intrathoracic organs and tissues. Consequently, surface potentials are increased, because the short circuit effect in thorax decreases.

The position of the diaphragm also changes during the parabolic flight.<sup>27</sup> During mild hypergravity it shifts downward, and during microgravity it shifts upward. The diaphragm has relatively high electroconductivity (in comparison to lung), and its changing position can lead to voltage change also.<sup>19</sup>

**Table 4.** Change of R Amplitude in Z During Microgravity with LBNP, Relative to Normogravity and Without LBNP

	Median	M	SD	Min	Max	N	P
Normogravity							
Decrease							
mV	−0.18	−0.2	0.17	−0.8	−0.02	18	NS
%	−11	−13	7.8	−30	−2	(69%)	
Increase							
mV	0.04	0.04	0.03	0.02	0.06	1	NS
%	2.6	2.6	1.6	3.8	3.75	(4%)	
Without LBNP							
Decrease							
mV	−0.03	−0.04	0.03	−0.09	−0.01	0	
%	−2.6	−3	2.4	−6	−0.7		
Increase							
mV	0.08	0.12	0.12	0.01	0.46	14	NS
%	4.3	5.3	4	0.4	1.4	(54%)	

M: mean; SD: standard deviation; N: number of cases with statistically significant changes.



**Table 5.** Change of R Amplitude in Z During Hypergravity and Microgravity, Relative to Normogravity in Supine Position

	Median	M	SD	Min	Max
Hypergravity					
Increase					
mV	0.03	0.03	0.02	0.01	0.05
%	3.9	3.5	1.8	0.9	5.3
Decrease					
mV	-0.02	-0.04	0.05	-0.11	0.01
%	-2.1	-5.7	8.3	-18	-5.5
Normogravity					
Increase					
mV	0.015	0.015	0.007	0.01	0.02
%	1.9	1.9	1.9	0.5	2.7
Decrease					
mV	-0.06	-0.05	0.03	-0.09	-0.01
%	-4.9	-6.3	4.9	-15.8	-2.1

*Second factor.* A significant factor is the short circuit effect in the heart itself, caused by "additional" blood during microgravity. The increased venous return during microgravity results in the increase of cardiac cavity volumes and internal surfaces of the heart. This allows for contacts of more surface with the highly conductive blood as the adjacent medium.<sup>34</sup> The absence of gravity reduces the downward stretching of the heart and the squeezing of intracardiac vessels and allows for a passive increase of the capacity of myocardial vessels surrounded by myocardial fibers.<sup>1</sup> This increased amount of blood in the heart walls results in decreased ECG voltage<sup>1</sup> as shown by the decrement of Rz amplitude in microgravity. The short circuit effect increases during microgravity. During mild hypergravity the venous return decreases, the heart cavity volumes and cardiac internal surface are all reduced, so that fewer fibers are in contact with highly conductive blood.<sup>34</sup> The heart stretches downward and blood is pressed out from heart wall as a result of squeezing of the cardiac vessels. A decreasing amount of blood in the heart wall results in increased ECG voltage<sup>1</sup> as shown by the increment of Rz amplitude in hypergravity.

The short circuit effect decreases in hypergravity. Consequently, the first and second factors act in the same way. Increase/decrease of the amount of blood in the lung and other intrathoracic organs, or in the heart wall and in the ventricles exhibits the same effect on QRS voltage. Increase is the amount of blood, e.g., during microgravity, results in an in-

crease in the short circuit effect. Decrease of the amount of blood, e.g., during mild hypergravity, results in decrease in the short circuit effect.

Application of LBNP in upright subjects in microgravity phase reduces the changes in the distribution of blood. As a result, changes in Rz amplitude are also limited. In the supine position there is no significant changes in blood distribution and there is no significant change of Rz amplitude.

*Third and fourth factors:* The chest form, heart position, form, and volume change during variations of gravity. This fact was also observed by other researchers under different clinical and experimental conditions.<sup>2,6-8,11,12,14,34-36</sup> The influence of these changes varies in different leads as shown in our study. Different changes in X and Z are attributed by some authors to the Brody effect.<sup>2,6-8</sup> In other publications it is explained by the position of the lung relative to the heart,<sup>11</sup> or by different modifications of the cardiac dipole in radial and transversal directions.<sup>12,14,34,35</sup> McFee and Rush<sup>14</sup> and Roberts et. al.<sup>35</sup> have noted that resistance of the heart muscle is lower in the direction of the fibers compared to that in the transversal direction. Hence, the influence of change of the heart muscle's electrical resistance—in our case during parabolic flight—can differ in different leads. Especially, fibers of apex and base can change differently during gravity-induced alteration from spherical to stretched and vice versa. Consequently, resistance of the heart muscle can influence surface potential differently in the apex (Rx) and at the base (Rz) of the heart. Khatib and Lab<sup>39</sup> examined the differences in

electrical activity in the apex and in the base at the instant of heart rate change and noted that these regional differences may be secondary to differences in wall dynamics. In this case the fibers of the apex and base stretch differently and the squeezing of vessels by surrounding myocardial fibers varies. It can induce differences in short circuiting between the apex and the base, resulting in differences in ECG changes between both regions.

Changes in chest form, heart position, form, and volume are accompanied by changes of distance between the surface of heart and the ECG electrodes. Under the normal gravity condition surface potentials increase parallel to volume increment, and the influence of nonhomogeneity is less than the influence of distance between electrodes and heart surface.<sup>13</sup> By using an equation from Voukidis et al.<sup>40</sup> we can evaluate the contribution of the Brody effect on the total change of surface potential during the parabolic flight. In different phases of the parabolic flight left ventricular volume changes do not exceed 10–30%; hence the magnitude of dipole vector changes as a consequence of Brody's effect does not exceed 3%.

Feldman et al.<sup>38</sup> showed that R wave amplitude increases as the left ventricular lateral wall moves closer to the V5, V6 electrodes (V5, V6 corresponding to X in the Frank lead system). In our study some of the electrodes, which form lead X, are disposed near the heart apex. During the microgravity phase these electrodes are more sensitive to change in heart position and form. The distance between the heart and electrodes decreases and Rx magnitude increases.

During a mild hypergravity phase the heart stretches downward and heart volume decreases (Table 3) so that heart horizontal size (front-back and right-left size) decreases. Consequently, distance between heart surface and electrodes, which form lead Z (and X too), increases. As a result of this, voltage in Z is expected to decrease. But in spite of the increment in the distance between the heart surface and Z-electrodes, magnitude R in Z increases. Apparently, in Z lead the distance factor is less significant than of short circuiting by blood. It is important to realize that during mild hypergravity the heart rate increases. Wakimoto et al.<sup>37</sup> showed that heart rate increase is accompanied by the increase of QRS amplitude, significantly in leads V2–V4, and nonsignificantly in lead V5. Others explained these results by the proximity effect described by Feldman et al.,<sup>38</sup> making the hypothesis that "LV chamber size decreases during

the tachycardia, the unfixed LV chamber may be forced to move anteriorly toward the aortic root, which is an anteriorly located, fixed anatomic structure," V2–V3 correspond to Z in the Frank lead system but the change in Z amplitude during mild hypergravity in the parabolic flight cannot be explained by this fact. During the microgravity phase heart rate and Z amplitude decrease, but the decrease in heart rate has been observed 1–3 seconds after the beginning of microgravity, whereas Z amplitude decrease is synchronous with the onset of microgravity. It means that the change in Z amplitude in our experiment correlates with heart rate but it was not determined by heart rate itself. The two effects are cumulative.

Ishikawa et al.<sup>34</sup> have analyzed their results of ECG change due to circulating blood volume change with consideration for the short circuit effect. They have noted that the influence of the short circuit effect is more expressed in R of Z lead and S of X lead. In our study Sx is not stable in difference from Rz. In mild hypergravity, Sx increases in 22% of cases, decreases in 17%, and does not change in 61% of cases. In microgravity, Sx increases in 35% of cases, decreases in 43%, does not change in 22% of cases.

Lepeshkin<sup>1</sup> has noted that the influence of tissue electroconduction must be manifested in last period of ventricular depolarization, when potential interextinction from different parts of myocardium is absent. This period corresponds to depolarization of back-basal region; in Frank ECG lead system it corresponds to wave R in Z. Our results confirm this supposition: most expressed steady voltage QRS changes take place in R amplitude change in Z.

The results of the experiments with LBNP and changes of body position (from upright to supine) confirmed this conclusion. During microgravity the volume of blood in thorax increases. The use of LBNP during microgravity reduces the increment of this volume. As a result, changes of ECG parameters are less expressed. Influence of LBNP on QRS voltage in microgravity in comparison to microgravity without LBNP is similar to the effects of hemorrhage and blood filling described by Manoach et al.<sup>3,5,41</sup>

With subjects in supine position during the parabolic flight the redistribution of blood is less expressed, the chest wall shape is more affected by the abdominal viscera movement, and gravity acts only upon the antero-posterior diameter of the thorax. As a result, ECG changes are not expressed.

The variations of amplitude values in our material from one subject in different campaigns can be explained by small changes in body or electrode positions. These small changes cannot explain exceptions from regularities. For R amplitude in Z there is one exception in campaign 1. This exception for the same subject did not appear in campaign 2, despite an analogical experiment set-up. Apparently, the influence of sporadic factors exists in several parabolas. Regularities for mean values take place in all cases.

It is necessary that if the first and second factors act to one direction in the study condition, the third factor act contrary to them. It leads to an underestimation of the real influence of electroconduction change. But our results show that even in this case the influence of thorax electroconduction change is significant.

In conclusion of our study we note following:

- I. Changes of QRS voltage during the parabolic flight can be attributed to the balance of two factors:
  - (a) Changes of the degree of short circuiting by variations in the amount of blood in thorax, i.e., in cardiac cavity, cardiac wall, intrathoracic organs, and tissues. The main effect is on R in the Z lead.
  - (b) Changes of distance between the heart and the electrodes as a result of change in the position, form, and volume of the heart. The superiority of this factor on the changes of the degree of short circuiting can be observed on R in the X lead.
- II. Changes of intrathoracic organs and tissue electroconduction have a significant influence on amplitude R in Z:
  - (a) increment in hypergravity (an average 0.19 mV in our study);
  - (b) decrement in microgravity (an average 0.24 mV in our study).

The influence of changes of distance between the heart and the electrodes can underestimate the real voltage changes in the consequence of intrathoracic organs and tissues electroconduction change, but does not exaggerate, and study results can be estimation of these changes from below.

**Acknowledgments:** We acknowledge the support from the Centre National d'Etudes Spatiales (CNES), the European Space Agency (ESA), the Conseil Régional d'Aquitaine and from Gagarin Cosmonauts' Training Center in Star City, Russia. We acknowledge the dedi-

icated collaboration of the crews of CNES AIRBUS A300 ZERO-G and IL-76 MDK. The support of the Cardionics Society, in particular Jean Waldura, is acknowledged with gratitude.

## REFERENCES

1. Lepeshkin E. Physiological influence on transfer factors between heart currents and body-surface potentials. In: Nelson CV, Geselowitz DB (eds.): *The Theoretical Basis of Electrocardiology*. Oxford, Clarendon, 1976, pp. 135–164.
2. Nelson CV. The influence of thorax dimensions and intracardiac blood on the vectorcardiogram In: Kneppo P (eds.): *Measuring and Modeling of the Cardiac Electrical Field*. Bratislava: Publishing House of the Slovak Academy of Sciences, 1980, pp. 193–199.
3. Manoach M, Gitter S, Grossman E, et al. The relation between the conductivity of blood and the body tissue and the amplitude of the QRS during heart filling and precordial compression in the cat. *Am Heart J* 1972;84:72–75.
4. Baybe RH, Kalbfleisch JH, Berry PM. Changes in the body's QRS surface potentials produced by alteration in certain compartment of the nonhomogeneous conducting model. *Am Heart J* 1969;77:517–519.
5. Manoach M, Gitter S, Grossman E. Some considerations regarding the importance of blood, heart and tissue conductivity with regard to QRS amplitude changes after hemorrhage. *Am Heart J* 1971;81:726–728.
6. Nelson CV, Chatterjee M, Angelakos ET, et al. Model studies on the effect of the intracardiac blood on the electrocardiogram. *Am Heart J* 1961;62:83–92.
7. Oretto G, Luzzo F, Donato A, et al. Electrocardiographic changes associated with haematocrit variations. *Eur Heart J* 1992;13:634–637.
8. Nelson CV, Rand PW, Angelakos ET, et al. Effect of intracardiac blood on the spatial vectorcardiogram. I. Results in the dog. *Circ Res* 1972;31:95–98.
9. Kilty SE, Lepeshkin E. Effect of body build on the QRS voltage of the electrocardiogram in normal men. Its significance in the diagnosis of left ventricular hypertrophy. *Circulation* 1965;31:77–84.
10. Rosenthal A, Restieaux NJ, Feig SA. Influence of acute variations in haematocrit on the QRS complex of the Frank electrocardiogram. *Circulation* 1971;44:456–465.
11. Rudy Y, Wood R, Plonsey R, et al. The effect of high lung conductivity on electrocardiographic potentials. Results from human subjects undergoing bronchopulmonary lavage. *Circulation* 1982;65:440–445.
12. Vitolo E, Madoi S, Palvarini M, et al. Relationship between changes in R-wave voltage and cardiac volume. A vectorcardiographic study during haemodialysis. *J Electrocardiol* 1987;20:138–146.
13. Amore JN. The Brody effect and changes of volume of the heart. *J Electrocardiol* 1985;18:71–76.
14. McFee R, Rush S. Qualitative effect of thoracic resistance variations on the interpretation of electrocardiograms: the low resistance surface layer. *Am Heart J* 1968;76:48–61.
15. Battler A, Froelicher V, Slutsky R, et al. Relationship of QRS amplitude changes during exercise to left ventricular function and volume and the diagnosis of coronary artery disease. *Circulation* 1979;60:1004–1013.
16. Simoons ML. Exercise electrocardiography and exercise testing. In Macfarlane PW, Lawrie TDV (eds.): *Comprehensive Electrocardiology. Theory and Practice in Health and Disease*. New-York, Pergamon Press, 1989, pp. 1107–1138.
17. Wolthuis RA, Froelicher V, Hopkirk A, et al. Normal electrocardiographic waveform characteristics during treadmill exercise testing. *Circulation* 1979;60:1028–1035.

18. David D, Naito M, Chen C, et al. R-wave amplitude variations during acute experimental myocardial ischemia: An inadequate index for changes in intracardiac volume. *Circulation* 1981;63:1364-1371.
19. Ruttkay-Nedetski I. Influence of breathing and heart position in chest in heart electrical field. In: Nelson CV, Geselowitz DB (eds.): *The Theoretical Basis of Electrocardiology*. Clarendon, Oxford, 1976, pp. 119-134.
20. Hoffman BF, Cranefield PF. *Electrophysiology of the Heart*. New York, McGraw-Hill, 1960.
21. Penefsky ZJ, Hoffman BF. Effect of stretch on mechanical and electrical properties of cardiac muscle. *Am J Physiol* 1963;204:433-438.
22. Lab MJ. Mechanically dependent changes in action potentials recorded from the intact frog ventricle. *Circ Res* 1978;42:519-528.
23. Lab MJ. Contraction-excitation feedback in myocardium. Physiological basis and clinical relevance. *Circ Res* 1982;50(6):757-766.
24. Schlegel TT, Benavides EW, Barker DC, et al. Cardiovascular and Valsalva responses during parabolic flight. *J Appl Physiol* 1998;85:1957-1965.
25. Bailliar O, Capderou A, Cholley BP, et al. Changes in lower limb volume in humans during parabolic flight. *J Appl Physiol* 1998;85:2100-2105.
26. Capderou A, Bailliar O, Maison-Blanche P, et al. Parasympathetic activity during parabolic flight, Effect of LBNP during microgravity. *Aviat Space Environ Med* 2001;72:361-367.
27. Paiva M, Estenne M, Engel LA. Lung volumes, chest wall configuration, and pattern of breathing in microgravity. *J Appl Physiol* 1989;67:1542-1550.
28. Macfarlane PW. Lead system. In Macfarlane PW, Lawrie TDV (eds.): *Comprehensive Electrocardiology. Theory and Practice in Health and Disease*. New York, Pergamon Press, 1989, pp. 316-352.
29. Whinnery YE. Acceleration induced voltage variations in the electrocardiogram during exhaustive simulated aerial combat maneuvering. *Aviat Space Environ Med* 1982;53:147-152.
30. Tzvetkov IA. Acceleration in flight and influence of them on human organism. In Babichuk AN (ed.): *Aviation Medicine*. Moscow, Publishing House "DOSAAF," 1980, pp. 96-121 (in Russian).
31. Madias JE. Effect of changes in body weight and serum albumin levels on electrocardiographic QRS amplitudes. *Am J Cardiol* 2002;89:1233-1235.
32. Fortney S, Tankesley C, Lightfoot JT, et al. Cardiovascular responses to lower body negative pressure in trained and untrained older men. *J Appl Physiol* 1992;73:2693-2700.
33. Surawicz B. Effect of heart rate on QRS voltage: A simple relation that escape notes. *J Cardiovasc Electrophysiol* 2000;11:61-63.
34. Ishikawa K, Shirato C, Yanagisawa A. Electrocardiographic change due to sauna bathing. Influence of acute reduction in circulating blood volume on body surface potentials with special reference to the Brody effect. *Br Heart J* 1983;50:469-475.
35. Roberts DE, Hersh LT, Scher AM. Influence of cardiac fiber orientation on wave front voltage, conduction velocity, and tissue resistivity in the dog. *Circ Res* 1979;44:701-712.
36. Gulrajani RM, Roberge FA, Mailloux GE. The forward problem of electrocardiography. In Macfarlane PW, Lawrie TDV (eds.): *Comprehensive Electrocardiology. Theory and Practice in Health and Disease*. New York, Pergamon Press, 1989, pp. 197-236.
37. Wakimoto H, Izumida N, Asano Y, et al. Augmentation of QRS wave amplitudes in the precordial leads during narrow QRS tachycardia. *J Cardiovasc Electrophysiol* 2000;11:52-60.
38. Feldman T, Childers RW, Borow KM, et al. Change in ventricular cavity size: Different effect on QRS and T amplitude. *Circulation* 1985;72:495-501.
39. Khatib SY, Lab MJ. Differences in electrical activity in the apex and base of left ventricle produced by changes in mechanical conditions of contraction. *J Physiol* 1982;324:25-26.
40. Voukydis PC, Angelakos ET, Nelson CV. Electrical effects of a highly conductive mass inside the thorax. *Am Heart J* 1973;85:382-388.
41. Manoch M. On Brody effect and increase in QRS amplitude. *J Cardiovasc Electrophysiol* 2000;11:833.